DEPARTMENT OF THE AIR FORCE
59TH MEDICAL WING (AETC)
JOINT BASE SAN ANTONIO - LACKLAND TEXAS

31 JULY 2017

MEMORANDUM FOR SVGT
ATTN: CAPT DEVIN R BROADWATER

FROM: 59 MDW/SGVU

SUBJECT: Professional Presentation Approval

Your paper, entitled **Clinicopathologic Features and Clinical Outcome in Secondary Histiocytic Sarcomas, an Institutional Experience** presented at/published to **College of American Pathology Archives, College of American Pathology Annual Meeting 2017, Washington D.C. Oct. 8-11 2017** in accordance with MDWI 41-108, has been approved and assigned local file #**17286.**

Pertinent biographic information (name of author(s) title, etc.) has been entered into our computer file. Please advise us (by phone or mail) that your presentation was given. At that time, we will need the date (month, day and year) along with the location of your presentation. It is important to update this information so that we can provide quality support for you, your department, and the Medical Center commander. This information is used to document the scholarly activities of our professional staff and students, which is an essential component of Wilford Hall Ambulatory Surgical Center (WHASC) internship and residency programs.

Please know that if you are a Graduate Health Sciences Education student and your department has told you they cannot fund your publication, the 59th Clinical Research Division may pay for your basic journal publishing charges (to include costs for tables and black and white photos). We cannot pay for reprints. If you are a 59 MDW staff member, we can forward your request for funds to the designated Wing POC at the Chief Scientist's Office, Ms. Alice Houy, office phone: 210-292-8029; email address: alice.houy.civ@mail.mil.

Congratulations, and thank you for your efforts and time. Your contributions are vital to the medical mission. We look forward to assisting you in your future publication/presentation efforts.

Linda Steel-Goodwin

LINDA STEEL-GOODWIN, Col, USAF, BSC
Director, Clinical Investigations & Research Support

PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

INSTRUCTIONS

USE ONLY THE MOST CURRENT 59 MDW FORM 3039 LOCATED ON AF E-PUBLISHING

1. The author must complete page two of this form:
   a. In Section 2, add the funding source for your study [e.g., 59 MDW CRD Graduate Health Sciences Education (GHSE) (SG5 O&M); SG5 R&D; Tri-Service Nursing Research Program (TSNRP); Defense Medical Research & Development Program (DMRDP); NIH; Congressionally Directed Medical Research Program (CDMRP) ; Grants; etc.]

   b. In Section 2, there may be funding available for journal costs, if your department is not paying for figures, tables or photographs for your publication. Please state "YES" or "NO" in Section 2 of the form, if you need publication funding support.

2. Print your name, rank/grade, sign and date the form in the author's signature block or use an electronic signature.

3. Attach a copy of the 59 MDW IRB or IACUC approval letter for the research related study. If this is a technical publication/presentation, state the type (e.g. case report, QA/QI study, program evaluation study, informational report/briefing, etc.) in the "Protocol Title" box.

4. Attach a copy of your abstract, paper, poster and other supporting documentation.

5. Save and forward, via email, the processing form and all supporting documentation to your unit commander, program director or immediate supervisor for review/approval.

6. On page 2, have either your unit commander, program director or immediate supervisor:
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7. Submit your completed form and all supporting documentation to the CRD for processing to: usaf.jbsa.59-mdw.mbx.wing-crd-publications-and-presentations@mail.mil. **This should be accomplished no later than 30 days before final clearance is required to publish/present your materials.** If you have any questions or concerns, please contact the 59 CRD/Publications and Presentations Section at 292-7141 for assistance.

8. The 59 CRD/Publications and Presentations Section will route the request form to clinical investigations, 502 ISG/JAC (Ethics Review) and Public Affairs (59 MDW/PA) for review and then forward you a final letter of approval or disapproval.

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11. The Joint Ethics Regulation (JER) DoD 5500.07-R, *Standards of Conduct*, provides standards of ethical conduct for all DoD personnel and their interactions with other non-DoD entities, organizations, societies, conferences, etc. Part of the Form 3039 review and approval process includes a legal ethics review to address any potential conflicts related to DoD personnel participating in non-DoD sponsored conferences, professional meetings, publication/presentation disclosures to domestic and foreign audiences, DoD personnel accepting non-DoD contributions, awards, honoraria, gifts, etc. The specific circumstances for your presentation will determine whether a legal review is necessary. **If you (as the author) or your supervisor check "NO" in block 17 of the Form 3039, your research or technical documents will not be forwarded to the 502 ISG/JAC legal office for an ethics review.** To assist you in making this decision about whether to request a legal review, the following examples are provided as a guideline:

    For presentations before professional societies and like organizations, the 59 MDW Public Affairs Office (PAO) will provide the needed review to ensure proper disclaimers are included and the subject matter of the presentation does not create any cause for DoD concern.

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NOTE: All abstracts, papers, posters, etc., should contain the following disclaimer statement:
"The views expressed are those of the [author(s)] [presenter(s)] and do not reflect the official views or policy of the Department of Defense or its Components"

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"The voluntary, fully informed consent of the subjects used in this research was obtained as required by 32 CFR 219 and DODI 3216.02_AFI 40-402."

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PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

1. TO: CLINICAL RESEARCH	2. FROM: (Author's Name, Rank, Grade, Office Symbol)	3. GME/GHSE STUDENT:	4. PROTOCOL NUMBER:
	Broadwater, Devin R, Capt, 0-3, SVGT	☒ YES ☐ NO	N/A

5. PROTOCOL TITLE: (**NOTE:** For each new release of medical research or technical information as a publication/presentation, a new 59 MDW Form 3039 must be submitted for review and approval.)

Case Study

6. TITLE OF MATERIAL TO BE PUBLISHED OR PRESENTED:

Clinicopathologic features and clinical outcome in secondary histiocytic sarcomas, an institutional experience.

7. FUNDING RECEIVED FOR THIS STUDY? ☐ YES ☒ NO FUNDING SOURCE:

8. DO YOU NEED FUNDING SUPPORT FOR PUBLICATION PURPOSES: ☐ YES ☒ NO

9. IS THIS MATERIAL CLASSIFIED? ☐ YES ☒ NO

10. IS THIS MATERIAL SUBJECT TO ANY LEGAL RESTRICTIONS FOR PUBLICATION OR PRESENTATION THROUGH A COLLABORATIVE RESEARCH AND DEVELOPMENT AGREEMENT (CRADA), MATERIAL TRANSFER AGREEMENT (MTA), INTELLECTUAL PROPERTY RIGHTS AGREEMENT ETC.?
☐ YES ☒ NO **NOTE:** If the answer is YES then attach a copy of the Agreement to the Publications/Presentations Request Form.

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CHECK APPROPRIATE BOX OR BOXES FOR APPROVAL WITH THIS REQUEST. ATTACH COPY OF MATERIAL TO BE PUBLISHED/PRESENTED.

☐ 11a. PUBLICATION/JOURNAL (List intended publication/journal.)

☒ 11b. PUBLISHED ABSTRACT (List intended journal.)
College of American Pathology Archives

☒ 11c. POSTER (To be demonstrated at meeting: name of meeting, city, state, and date of meeting.)
College of American Pathology Annual Meeting 2017, Washington D.C., Oct 8-11 2017

☐ 11d. PLATFORM PRESENTATION (At civilian institutions: name of meeting, state, and date of meting.)

☐ 11e. OTHER (Describe: name of meeting, city, state, and date of meeting.)

12. HAVE YOUR ATTACHED RESEARCH/TECHNICAL MATERIALS BEEN PREVIOUSLY APPROVED TO BE PUBLISHED/PRESENTED?
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DATE	

14. 59 MDW PRIMARY POINT OF CONTACT (Last Name, First Name, M.I., email)	15. DUTY PHONE/PAGER NUMBER
Broadwater, Devin, R. devin.r.broadwater.mil@mail.mil	334-477-8576

16. AUTHORSHIP AND CO-AUTHOR(S) List in the order they will appear in the manuscript.

LAST NAME, FIRST NAME AND M.I.	GRADE/RANK	SQUADRON/GROUP/OFFICE SYMBOL	INSTITUTION (If not 59 MDW)
a. Primary/Corresponding Author Broadwater, Devin R	O-3/Capt	959 CSPS/SVGT	
b. Wei, Shi	Civilian	N/A	UAB
c. Peker, Deniz	Civilian	N/A	UAB
d.			
e.			

17. IS A 502 ISG/JAC ETHICS REVIEW REQUIRED (JER DOD 5500.07-R)? ☐ YES ☒ NO

I CERTIFY ANY HUMAN OR ANIMAL RESEARCH RELATED STUDIES WERE APPROVED AND PERFORMED IN STRICT ACCORDANCE WITH 32 CFR 219, AFMAN 40-401_IP, AND 59 MDWI 41-108. I HAVE READ THE FINAL VERSION OF THE ATTACHED MATERIAL AND CERTIFY THAT IT IS AN ACCURATE MANUSCRIPT FOR PUBLICATION AND/OR PRESENTATION.

18. AUTHOR'S PRINTED NAME, RANK, GRADE	19. AUTHOR'S SIGNATURE	20. DATE
Devin Broadwater, Capt, O-3	BROADWATER.DEVIN.R.1179041827 Digitally signed by BROADWATER.DEVIN.R.1179041827 Date: 2017.07.20 06:40:40 -05'00'	July 20, 2017
21. APPROVING AUTHORITY'S PRINTED NAME, RANK, TITLE	**22. APPROVING AUTHORITY'S SIGNATURE**	**23. DATE**
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PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

1st ENDORSEMENT (59 MDW/SGVU Use Only)

TO: Clinical Research Division 59 MDW/CRD Contact 292-7141 for email instructions.	24. DATE RECEIVED July 20, 2017	25. ASSIGNED PROCESSING REQUEST FILE NUMBER 17286

26. DATE REVIEWED	27. DATE FORWARDED TO 502 ISG/JAC
27 Jul 2017	

28. AUTHOR CONTACTED FOR RECOMMENDED OR NECESSARY CHANGES: ☐ NO ☒ YES If yes, give date. 27 Jul 2017 ☐ N/A

29. COMMENTS ☒ APPROVED ☐ DISAPPROVED

The author submitted the IRB approval letter. The abstract and presentation are approved.

30. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER	31. REVIEWER SIGNATURE	32. DATE
Rocky Calcote, PhD, Clinical Research Administrator	CALCOTE ROCKY.D.1178245844	

2nd ENDORSEMENT (502 ISG/JAC Use Only)

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36. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER	37. REVIEWER SIGNATURE	38. DATE

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39. DATE RECEIVED	40. DATE FORWARDED TO 59 MDW/SGVU
July 28, 2017	July 28, 2017

41. COMMENTS ☒ APPROVED (In compliance with security and policy review directives.) ☐ DISAPPROVED

42. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER	43. REVIEWER SIGNATURE	44. DATE
Kevin Iinuma, SSgt/E-5, 59 MDW Public Affairs	IINUMA.KEVIN.MITSUGU.1296227613	July 28, 2017

4th ENDORSEMENT (59 MDW/SGVU Use Only)

45. DATE RECEIVED	46. SENIOR AUTHOR NOTIFIED BY PHONE OF APPROVAL OR DISAPPROVAL ☐ YES ☐ NO ☐ COULD NOT BE REACHED ☐ LEFT MESSAGE

47. COMMENTS ☐ APPROVED ☐ DISAPPROVED

48. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER	49. REVIEWER SIGNATURE	50. DATE

Clinicopathologic features and clinical outcomes in secondary histiocytic sarcomas, an institutional experience.

Devin R. Broadwater, M.D.[1], Shi Wei, M.D.[2], Deniz Peker, M.D., FCAP[2]

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Department of Pathology, University of Alabama at Birmingham, Birmingham, AL, United States.

Context

Histiocytic Sarcoma is an extraordinarily rare neoplasm with very few case reports and case series published in the literature. Currently, the tumor has an unknown etiology and often presents at extranodal sites. Morphologically, the tumor is often a diffuse non-cohesive proliferation of large cells that can be either monomorphic or pleomorphic. These tumors are often diagnosed by immunohistochemistry by establishing histiocytic lineage through CD163 and CD68. Additionally, HS are positive for lysozyme. Cells are typical absent of other histiocytic and dendritic cell neoplasm markers including Langerhans cells (CD1a, langerin), follicular dendritic cells (CD21, CD35), and myeloid cells (CD33, CD13, myeloperoxidase). CD45 may be positive, and S-100 may be focally positive. The undifferentiated morphology and difficult staining pattern leads to poor diagnostic yields. The vast majority of patients die from disease progression.[1-2] To date there is no optimal treatment regiment for HS, with only a few case reports and occasional case series discussing treatment regiments prescribed with varying degrees of success. [3-8]

At present, little has been established for HS. Particularly, while overall survival is known to be low, there is no literature remarking on survival in different populations. In this study, patients with de novo histiocytic sarcomas were compared to patients with secondary histiocytic sarcoma after chemotherapy or radiotherapy.

The purpose of this study was to illustrate demographics on patients with Histiocytic sarcomas, review key immunohistiochemical stains to establish diagnosis, and compare de novo to secondary histiocytic sarcoma

Design

- Institutional Review Board approved retrospective study
- Patients with Histiocytic Sarcoma diagnosed and treated at UAB between 1 Jan 2004 and 31 Dec 2016 were identified
- Cases were categorized by primary histiocytic sarcoma and secondary (defined as prior cancer diagnosis and received treatment followed by diagnosis of histiocytic sarcoma)
- Clinical data was gathered through the electronic medical record
- Pathological slides were reviewed for histopathologic, and immunophenotypic data
- Data gathered from identified cases was compared

Results

- 18 cases identified, see **Table 1**
- Mean age wasa 57 years (5-84)
- Male:Female ration was 0.8 (M:8, F:10)
- Five patients had history of prior unrelated malignancy treated with chemotherapy or radiotherapy (Secondary HS) with a mean delay of 33 months between treatment and diagnosis (12 to 60)
- The majority of HS was treated with surgery (83%) followed by chemotherapy (22%)
- The majority of patients received surgery as their only treatment (67%)
- Overall survival was 44 months
- De novo HS overall survival was 64 months compared with 12.8 months of secondary HS [mean survival difference = 51 months (95% CI, 3 to 100), p=0.0386]

Table 1. Patients with new diagnosis of histiocytic sarcoma.

Pt #	Age (Years)/Sex	Location	Prior Therapy	OS (Months)
1	72 / F	Liver	CTX	0
2	84 / M	Larynx	None	23
3	79 / M	Lung	XRT + CTX	39
4	52 / M	Thigh	None	146
5	22 / F	Forearm	None	130
6	79 / F	Leg	None	116
7	66 / F	Breast	XRT	15
8	77 / M	Scalp and adrenal gland	None	3
9	58 / F	Mediastinum	None	9
10	62 / M	Scalp	CTX	8
11	55 / M	Peg tube region	XRT + CTX	1
12	80 / F	Soft palate	None	77
13	5 / F	Orbit	None	79
14	17 / M	Lung	None	79
15	72 / F	Leg	None	27
16	58 / F	Lung	None	28
17	51 / F	Pancreas	None	1
18	34 / M	Left arm, soft tissue	None	6

Abbreviations: Pt = Patient, F= Female, M = Male, CTX = Chemotherapy, XRT = Radiotherapy, OS = Overall Survival

Conclusion

- **The clinical presentation of histiocytic sarcoma is often nonspecific and not considered in the clinical differentiation**
- **Thorough morphologic and immunophenotypic evaluation is warranted to establish an accurate diagnosis, especially use of CD 163 and CD 68 in otherwise unspecific immunohistiochemical staining patterns**
- **Low overall survival in all patients suggest more aggressive management is needed**
- **The shorter overall survival of secondary histiocytic sarcoma suggest a more aggressive malignancy than de novo disease**
- **Larger studies are needed to further investigate the biology and genetics of the disease**

References

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Clinicopathologic features and clinical outcomes in secondary histiocytic sarcomas, an institutional experience

Devin Broadwater, M.D.,[2] Shi Wei, M.D., Ph.D.,[1] Deniz Peker, M.D.[1]

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Abstract

Context: Histiocytic sarcomas (HS) are rare, often presenting with undifferentiated morphology and phenotype, resulting in poor diagnostic yield. Once diagnosed, clinical treatments lead to indeterminate outcomes. This institutional experience explores clinicopathologic features of de novo and secondary HS.

Design: A retrospective study was conducted following Institutional Board Review. Clinical, histopathologic, and immunophenotypic data were collected from patients diagnosed and treated at University of Alabama at Birmingham from 2004 to 2016.

Results: There were 18 cases identified. Mean age was 57 years (5 to 84) and male:female ratio was 0.8 (M:8, F:10). The cases included 18 HS (Table 1), five of which with a history of unrelated malignancies treated with chemotherapy or radiotherapy, with a mean delay of 33 months (12 to 60 months). The majority of HS was treated with surgery (62%), followed by chemotherapy (35%), with an overall survival of 44 months. The overall survival of de novo HS was 64 months compared with 12.8 months of secondary HS. The mean survival difference between de novo and secondary HS was significant [51 months (95% CI, 3 to 100), p =0.0386].

Conclusion: The shorter overall survival of secondary HS suggests a more aggressive malignancy than de novo disease. Larger scale studies are needed to further investigate the biology and genetics of the disease.

Table 1. Sample patients with new diagnosis of histiocytic sarcoma.

Pt #	Age (Years)/Sex	Location	Prior Therapy	OS (Months)
1	72 / F	Liver	CTX	0
2	84 / M	Larynx	None	23
3	79 / M	Lung	XRT + CTX	39
4	52 / M	Thigh	None	146
5	22 / F	Forearm	None	130
6	79 / F	Leg	None	116
7	66 / F	Breast	XRT	15
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9	58 / F	Mediastinum	None	9
10	62 / M	Scalp	CTX	8
11	55 / M	Peg tube region	XRT + CTX	1
12	80 / F	Soft palate	None	77
13	5 / F	Orbit	None	79
14	17 / M	Lung	None	79
15	72 / F	Leg	None	27
16	58 / F	Lung	None	28
17	51 / F	Pancreas	None	1
18	34 / M	Left arm, soft tissue	None	6

Abbreviations: Pt = Patient, F= Female, M = Male, CTX = Chemotherapy, XRT = Radiotherapy, OS = Overall Survival